```
     (FILE 'HOME' ENTERED AT 09:48:36 ON 13 DEC 2006)

     FILE 'CAPLUS' ENTERED AT 09:49:22 ON 13 DEC 2006
L1           213 S OMEPRAZOLE(L)MODEL
L2            21 S L1 AND (ANIMAL(W)MODEL)
L3             0 S L2 AND ((SERUM OR PLASMA)(L)CONCEN?)
L4             0 S L1 AND ((SERUM OR PLASMA)(L)CONCEN?)
L5            11 S OMEPRAZOLE(L)((SERUM OR PLASMA)(L)CONCEN?)
L6             0 S L5 AND L2

     FILE 'STNGUIDE' ENTERED AT 09:52:37 ON 13 DEC 2006

     FILE 'CAPLUS' ENTERED AT 09:58:15 ON 13 DEC 2006

     FILE 'STNGUIDE' ENTERED AT 09:59:13 ON 13 DEC 2006

     FILE 'CAPLUS' ENTERED AT 10:07:21 ON 13 DEC 2006
L7           163 S OMEPRAZOLE(L)ABSORPTION
L8            72 S L7 AND (PLASMA OR SERUM)
L9            15 S L8 AND PY<1996

     FILE 'STNGUIDE' ENTERED AT 10:11:56 ON 13 DEC 2006
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=> d bib hit 1-15

L9 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1995:822736 CAPLUS
DN 123:237674
TI Rectal absorption of omeprazole from suppositories in rabbits
AU Eun, Kyong-Hoon; Lee, Yong-Hee; Shim, Chang-Koo
CS College Pharmacy, Seoul National University, Seoul, 151-742, S. Korea
SO Archives of Pharmacal Research (1995), 18(4), 219-23
CODEN: APHRDQ; ISSN: 0253-6269
PB Pharmaceutical Society of Korea
DT Journal
LA English
TI Rectal absorption of omeprazole from suppositories in rabbits
SO Archives of Pharmacal Research (1995), 18(4), 219-23
CODEN: APHRDQ; ISSN: 0253-6269
AB Rectal absorption of omeprazole, a proton pump inhibitor, from suppositories was studied in rabbits. The suppositories were prepared by the conventional melting method with two types of bases, water-soluble PEG 4000 and oil-soluble Witepsol H15 bases, and administered intrarectally (ir) to rabbits at a dose of 10 mg omeprazole/kg. The plasma omeprazole concentration-time profiles of the two suppositories were compared with those following i.v. administration of the same dose. There were no significant differences between the two suppositories in bioavailabilities and peak plasma concns. (Cmax). Bioavailabilities and Cmax of PEG- and Witepsol suppositories were 30.3 and 33.9%, and 7.0 and 5.6 μg/mL, resp. However, PEG suppository showed significantly ($P < 0.05$) shorter time to leach peak plasma concentration (Tmax), mean absorption time (MAT) and mean residence time in the plasma (MRT) than Witepsol suppository. The Tmax, MRT and MAT were 25.0, 83.0 and 38.5 min for PEG suppository, but were 90.0, 122.5 and 78.0 min for Witepsol suppository, resp. These differences between the two suppositories could be explained by the difference in the in vitro dissoln. rates between the suppositories. The dissoln. of omeprazole from PEG suppository was reportedly much faster than that from Witepsol suppository. It suggests that plasma profiles of omeprazole, especially Cmax, MAT and MRT, could be controlled by modifying the in vitro dissoln. rate of the drug from the suppositories. Above results suggest that rectal suppository is worth developing as an alternative dosage form of omeprazole to the conventional oral prepns. which need sophisticated treatments, such as enteric coating, to prevent acid degradation of the drug in the stomach fluid.
ST omeprazole absorption rectum suppository
IT Drug bioavailability
Solution rate
(rectal absorption of omeprazole from suppositories)
IT Glycerides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coco mono-, di- and tri-, hydrogenated, rectal absorption of omeprazole from suppositories)
IT Intestine
(rectum, rectal absorption of omeprazole from suppositories)
IT Pharmaceutical dosage forms
(suppositories, rectal absorption of omeprazole from suppositories)
IT 73590-58-6, Omeprazole
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(rectal absorption of omeprazole from suppositories)
IT 25322-68-3, Peg
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(rectal absorption of omeprazole from suppositories)

L9 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1995:728282 CAPLUS
DN 123:131956
TI Effects of an acidic beverage (Coca-Cola) on absorption of ketoconazole
AU Chin, Thomas W. F.; Loeb, Mark; Fong, Ignatius W.
CS Fac. Pharm., Univ. Toronto, Toronto, ON, Can.
SO Antimicrobial Agents and Chemotherapy (1995), 39(8), 1671-5
CODEN: AMACCQ; ISSN: 0066-4804
PB American Society for Microbiology
DT Journal
LA English
SO Antimicrobial Agents and Chemotherapy (1995), 39(8), 1671-5
CODEN: AMACCQ; ISSN: 0066-4804
AB Absorption of ketoconazole is impaired in patients with achlorhydria. The purpose of this study was to determine the effectiveness of a palatable acidic beverage (Coca-Cola Classic, pH 2.5) in improving the absorption of ketoconazole in the presence of drug-induced achlorhydria. A prospective, randomized, three-way crossover design with a 1-wk wash-out period between each treatment was employed. Nine healthy nonsmoking, nonobese volunteers between 22 and 41 yr old were studied. Each subject was randomized to receive three treatments: (A) ketoconazole 200-mg tablet with water (control), (B) omeprazole (60 mg) followed by ketoconazole (200 mg) taken with water, and (C) omeprazole (60 mg) followed by ketoconazole (200 mg) taken with 240 mL of Coca-Cola Classic. The pH values of gastric aspirates were checked after omeprazole was administered to confirm attainment of a pH of >6. Multiple serum samples were obtained for measurements of ketoconazole concns. by high-pressure liquid chromatog. The mean area under the ketoconazole concentration-time curve from zero to infinity for the control treatment (17.9 ± 13.1 mg·h/L) was significantly greater than that for treatment B (3.5 ± 5.1 mg·h/L; 16.6%% ± 15.0% of control). The mean area under the concentration curve was significantly increased with treatment C (11.2 ± 10.6 mg·h/L; 64.8% ± 29.7% of control). The mean peak concentration was highest for the control treatment (4.1 ± 1.9 μg/mL), compared with that for treatment B (0.8 ± 1.1 μg/mL) and that for treatment C (2.4 ± 1.7 μg/mL), for which the mean peak concentration showed a significant increase over that for treatment B.
The absorption of ketoconazole was reduced in the presence of omeprazole-induced achlorhydria. However, drug absorption was significantly increased, to approx. 65% of the mean for the control treatment, when the drug was taken with an acidic beverage, such as Coca-Cola.

L9 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1995:715548 CAPLUS
DN 123:101996
TI Bioavailabilities of omeprazole administered to rats through various routes
AU Choi, Mi-Sook; Lee, Young-Hee; Shim, Chang-Koo
CS Coll. Pharmacy, Seoul Natl. Univ., Seoul, 151-742, S. Korea
SO Archives of Pharmacal Research (1995), 18(3), 141-5
CODEN: APHRDQ; ISSN: 0253-6269
PB Pharmaceutical Society of Korea
DT Journal
LA English

SO Archives of Pharmacal Research (1995), 18(3), 141-5
CODEN: APHRDQ; ISSN: 0253-6269

AB Omeprazole, a proton pump inhibitor, was given i.v., orally (po), i.p., hepatoportalvenously (pv), and intrarectally (i.r.) to rats at a dose of 72 mg/kg in order to investigate the bioavailability of the drug. The extent of bioavailabilities of omeprazole administered through pv, i.p., po, and ir routes were 88.5, 79.4, 40.8, and 38.7%, resp. Pharmacokinetics anal. in this study and literature (Regardh et al., 1985: Watanabe et al., 1994) implied significant dose-dependency in hepatic first-pass metabolism, clearance and distribution, and acidic degradation in gastric fluid. The high bioavailability from the pv administration (88.5%) means that only 11.5% of dose was extracted by the first-pass metabolism through the liver at this dose (72 mg/kg). The low bioavailability from the oral administration (40.8%), in spite of minor hepatic first-pass extraction, indicates low transport of the drug from GI lumen to portal vein. From the literature (Pilbrant and Cederberg, 1985), acidic degradation in gastric fluid was considered to be the major cause of the low transport. Thus, enteric coating of oral prepns. would enhance the oral bioavailability substantially. The bioavailability of the drug from the rectal route, in which acidic degradation and hepatic first-pass metabolism may not occur, was low (38.7%), but comparable to that from the oral route (40.8%), indicating poor transport across the rectal membrane. In this case, addition of an appropriate absorption enhancer would improve the bioavailability. The rectal route seems to be a possible alternative to the conventional oral route for omeprazole administration.

ST omeprazole bioavailability pharmacokinetics administration route; intravenous oral intraperitoneal omeprazole bioavailability pharmacokinetics; hepatoportalvenous intrarectal omeprazole bioavailability pharmacokinetics; HPLC omeprazole blood plasma

L9 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1994:620985 CAPLUS
DN 121:220985
TI Omeprazole-induced increase in the absorption of bismuth from tripotassium dicitratobismuthate
AU Treiber, Gerhard; Walker, Siegfried; Klotz, Ulrich
CS Robert Bosch Foundation, Stuttgart, 70376, Germany
SO Clinical Pharmacology & Therapeutics (St. Louis, MO, United States) (1994), 55(5), 486-91
CODEN: CLPTAT; ISSN: 0009-9236
DT Journal
LA English
TI Omeprazole-induced increase in the absorption of bismuth from tripotassium dicitratobismuthate
SO Clinical Pharmacology & Therapeutics (St. Louis, MO, United States) (1994), 55(5), 486-91
CODEN: CLPTAT; ISSN: 0009-9236

AB Omeprazole is an effective drug for treating active peptic ulcer, whereas tripotassium dicitratobismuthate can prevent ulcer relapse if Helicobacter pylori is eradicated. Because both drugs will be given concomitantly, drug interactions have to be considered, especially since absorption of bismuth may be dependent on intragastric pH, which will be elevated by omeprazole. In a placebo-controlled crossover study, 6 healthy volunteers received daily oral doses of 40 mg omeprazole for 1 wk and a single oral dose of 240 mg tripotassium dicitrato bismuthate. Plasma concentration-time profiles (AUC) and urinary excretion (Ae) of bismuth were measured by atomic absorption spectrophotometry and plasma levels of omeprazole by HPLC. In addition, intragastric pH values were monitored for 8 h. The increase of intragastric pH was related to the AUC of omeprazole . Omeprazole increased absorption of bismuth because AUC and Ae were higher during omeprazole treatment (172 μg/L · hr and 1.9 mg/8 h, resp.,) compared with placebo (46 μg/L

· hr and 0.27 mg/8 h, resp.,). A significant correlation could be observed between intragastric pH differences and Ae values. Omeprazole increased the systemic availability of bismuth from tripotassium dicitratobismuthate. Whether this pharmacokinetic interaction between both drugs results in alterations of H. pylori eradication or the toxic potential of bismuth remains to be elucidated by further clin. studies.

ST omeprazole absorption bismuth tripotassium dicitratobismuthate

IT Drug bioavailability
(omeprazole-induced increase of bismuth absorption from tripotassium dicitratobismuthate in humans)

IT Drug interactions
(pharmacokinetic, omeprazole-induced increase of bismuth absorption from tripotassium dicitratobismuthate in humans)

IT 7440-69-9, Bismuth, biological studies 57644-54-9, Tripotassium dicitratobismuthate 73590-58-6, Omeprazole
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(omeprazole-induced increase of bismuth absorption from tripotassium dicitratobismuthate in humans)

L9 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1994:586991 CAPLUS

DN 121:186991

TI Doxycycline carrageenate - an improved formulation providing more reliable absorption and plasma concentrations at high gastric pH than doxycycline monohydrate

AU Grahnen, A.; Olsson, B.; Johansson, G.; Eckerneas, S. A.

CS Pharmaco Med. Consult. PMC AB, Uppsala, Swed.

SO European Journal of Clinical Pharmacology (1994), 46(2), 143-6
CODEN: EJCPAS; ISSN: 0031-6970

DT Journal

LA English

TI Doxycycline carrageenate - an improved formulation providing more reliable absorption and plasma concentrations at high gastric pH than doxycycline monohydrate

SO European Journal of Clinical Pharmacology (1994), 46(2), 143-6
CODEN: EJCPAS; ISSN: 0031-6970

AB The effect of increased gastric pH (obtained by pre-treatment with omeprazole) on the bioavailability of doxycycline monohydrate and doxycycline carrageenate has been investigated in 24 healthy volunteers, using an open, randomized, four-treatment, four-period, crossover, 2 + 2 factorial design. Each subject received a single dose of 100 mg of each of the doxycycline formulations with and without pre-treatment with omeprazole (40 mg daily for 7 days). The two formulations were bioequivalent (rate and extent) during fasting without omeprazole pre-treatment, whereas after omeprazole, the monohydrate showed a highly significant decrease in bioavailability (38 % for AUC and 45 % for Cmax) compared to the carrageenate formulation, which was not affected by prior administration of omeprazole. Many of the subjects did not reach a therapeutic plasma level of doxycycline during the combination of omeprazole and doxycycline monohydrate, and most adverse events (mainly gastrointestinal) were reported after this combination. As large populations of patients have a high gastric pH due to frequent use of H2-blockers, proton pump inhibitors and antacids, as well as to physiol. achlorhydria, the decreased absorption of doxycycline monohydrate may well have a clin. impact, for example when the patients are treated with tetracyclines for an infection.

IT 564-25-0 17086-28-1, Doxycycline monohydrate
RL: BIOL (Biological study)
(gastric absorption of, omeprazole effects on, pharmaceutical composition containing)

L9 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1994:315106 CAPLUS
DN 120:315106
TI Omeprazole therapy causes malabsorption of cyanocobalamin (vitamin B12)
AU Marcuard, Stefan P.; Albernaz, Lisa; Khazanie, Prabhaker G.
CS Sch. Med., East Carolina Univ., Greenville, NC, USA
SO Annals of Internal Medicine (1994), 120(3), 211-15
CODEN: AIMEAS; ISSN: 0003-4819
DT Journal
LA English
SO Annals of Internal Medicine (1994), 120(3), 211-15
CODEN: AIMEAS; ISSN: 0003-4819
AB Protein-bound cyanocobalamin (vitamin B12) absorption before and after omeprazole (Prilosec) therapy was evaluated in ten healthy male volunteers 22 to 50 yr old. Each volunteer served as his own control. Each participant had a modified Schilling test (protein-bound cyanocobalamin) and a gastric anal., as well as measurements of serum vitamin B12, gastrin, and folate levels. Five patients were then randomly assigned to take either 20 mg or 40 mg of omeprazole daily. After 2 wk of omeprazole therapy, these tests were repeated. At the end of the 2-wk treatment period, cyanocobalamin absorption decreased from 3.2% to 0.9% ($P = 0.031$) in participants receiving 20 mg of omeprazole daily. In patients taking 40 mg of omeprazole daily, cyanocobalamin absorption decreased from 3.4% to 0.4% ($P < 0.05$). Omeprazole therapy acutely decreased cyanocobalamin absorption in a dose-dependent manner.
IT 68-19-9, Vitamin B12
RL: BIOL (Biological study)
(absorption, omeprazole inhibition of, in humans)
IT 73590-58-6, Omeprazole
RL: BIOL (Biological study)
(cyanocobalamin absorption inhibition by, in humans)

L9 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1994:116676 CAPLUS
DN 120:116676
TI Bioequivalence of enteric-coated omeprazole products
AU Kim, Chong Kook; Jeong, Eun Ju; Lee, Eun Jin; Shin, Hee Jong; Lee, Won Keun
CS Coll. Pharm., Seoul Natl. Univ., Seoul, 151-742, S. Korea
SO Yakche Hakhoechi (1993), 23(1), 41-9
CODEN: YAHAEX; ISSN: 0259-2347
DT Journal
LA Korean
SO Yakche Hakhoechi (1993), 23(1), 41-9
CODEN: YAHAEX; ISSN: 0259-2347
AB The bioequivalence of two omeprazole (I) enteric-coated products was evaluated in 16 normal male volunteers following single oral administration. Test product was enteric-coated KD-182 tablet and reference product was Rosec capsule containing enteric-coated pellets of omeprazole. Both products contain 20 mg I. One tablet or capsule of the test or the reference product was administered to the volunteers, resp., by randomized two period cross-over study (2 + 2 Latin square method). Average drug concns. at each sampling time and pharmacokinetic parameters calculated were not significantly different between two products; the area under the concentration-time curve to last sampling time (8 h) (AUC0-8 hr) (1946.5 ± 675.3 vs 2018.3 ± 761.6 ng·hr/mL), AUC from time zero to infinite (AUC0-∞) (2288.6 ± 1212.8 vs 2264.9 ± 1001.3 ng·hr/mL), maximum plasma concentration (Cmax) (772.5 ± 283.3 vs 925.8 ± 187.7 ng/mL), time to maximum plasma concentration (Tmax) (2.38 ± 1.06 vs 2.34 ± 1.09 h), apparent elimination rate constant (ke) (0.5339 ± 0.2687 vs 0.5769 ± 0.2184 h-1), apparent

absorption rate constant (ka) (1.1536 ± 0.5278 vs 0.9739 ± 0.9507 h-1) and mean residence time (MRT) (3.13 ± 0.73 vs 3.41 ± 1.04 h). The differences of mean AUC0-8 hr, Cmax, Tmax and MRT between the two products (3.69, 19.83, 1.32 and 8.99%, resp.) were less than 20%. The power (1-β) and treatment difference (Δ) for AUC0-8 hr, Cmax and MRT were more than 0.8 and less than 0.2, resp. Although the power for Tmax was under 0.8, Tmax of the two products was not significantly different each other ($p > 0.05$). These results suggest that the bioavailability of KD-182 tablet is not significantly different from that of Rosec capsule. Therefore, two products are bioequivalent based on the current results.

L9 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1992:542847 CAPLUS
DN 117:142847
TI The effects of omeprazole-induced hypochlorhydria on absorption of theophylline from a sustained-release formulation
AU Sommers, De K.; Van Wyk, M.; Snyman, J. R.; Moncrieff, J.
CS Dep. Pharmacol., Univ. Pretoria, Pretoria, S. Afr.
SO European Journal of Clinical Pharmacology (1992), 43(2), 141-3
CODEN: EJCPAS; ISSN: 0031-6970
DT Journal
LA English
TI The effects of omeprazole-induced hypochlorhydria on absorption of theophylline from a sustained-release formulation
SO European Journal of Clinical Pharmacology (1992), 43(2), 141-3
CODEN: EJCPAS; ISSN: 0031-6970
AB The present study was designed to investigate the effects of raised intragastric pH on the absorption of theophylline from a sustained-release formulation. Six healthy male volunteers participated in the cross-over randomized study and on one of two occasions were pretreated with 240 mg omeprazole, administered in three divided doses over the 22 h preceding the test. The sulphasalazine/sulphapyridine method of assessing oral-cecal transit time was implemented in order to assess upper bowel and colonic absorption. The mean fraction absorbed - time profile was calculated from serial serum theophylline concentration measurements by a modification of the Wagner-Nelson equation. During hypochlorhydria the mean oral-cecal transit time was 4.6 h, mean time to 90% absorption 6.8 h, and the percentage theophylline presumably to be absorbed from the colon 32.3. The corresponding values with normochlorhydria were, resp., 3.8 h, 8.5 h, and 57.5%. The shorter oral-cecal transit time and lesser upper bowel absorption during normochlorhydria is postulated to result from motilin release due to duodenal acidification. Gastric hypoacidity resulted in significantly increased cumulative fractions of theophylline absorbed during a 3.5 h period, starting 0.5 h after breakfast. Possibility hypochlorhydria amplifies the increased motility which follows the intake of a meal, resulting in increased peristalsis and antiperistalsis, with more rapid drug absorption.

L9 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1992:227686 CAPLUS
DN 116:227686
TI Influence of single- and multiple-dose omeprazole treatment on nifedipine pharmacokinetics and effects in healthy subjects
AU Soons, P. A.; Van den Berg, G.; Danhof, M.; Van Brummelen, P.; Jansen, J. B. M. J.; Lamers, C. B. H. W.; Breimer, D. D.
CS Cent. Bio-Pharm., Univ. Leiden, Leiden, Neth.
SO European Journal of Clinical Pharmacology (1992), 42(3), 319-24
CODEN: EJCPAS; ISSN: 0031-6970
DT Journal
LA English
SO European Journal of Clinical Pharmacology (1992), 42(3), 319-24
CODEN: EJCPAS; ISSN: 0031-6970

AB The effects of single-dose (20 mg) and short-term (20 mg/day for 8 days) oral treatment with omeprazole on the pharmacokinetics and effects of oral nifedipine (10 mg capsule) and on gastric pH were investigated in a randomized, double-blind, placebo-controlled cross over study in nonsmoking healthy male subjects. The single dose of omeprazole had no effect on any pharmacokinetic parameter of nifedipine, or on gastric pH, blood pressure, or heart rate. Short-term omeprazole treatment increased the area under the plasma time-vs.-concentration curve of nifedipine by 26%, but all other pharmacokinetic parameters of nifedipine were not changed. The median gastric pH during the absorption phase of nifedipine was increased by short-term omeprazole (pH 4.2) compared to placebo treatment (pH 1.4). Blood pressure and heart rate did not differ between treatments. The interaction between nifedipine and omeprazole is not likely to be of major clin. relevance.

L9 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1992:15381 CAPLUS
DN 116:15381
TI Minor effect of multiple dose omeprazole on the pharmacokinetics of digoxin after a single oral dose
AU Oosterhuis, Berend; Jonkman, Jan H. G.; Andersson, Tommy; Zuiderwijk, Peter B. M.; Jedema, Jaap N.
CS Pharma Bio-Res. Int. B. V., Zuidlaran, 9470 AE, Neth.
SO British Journal of Clinical Pharmacology (1991), 32(5), 569-72
CODEN: BCPHBM; ISSN: 0306-5251
DT Journal
LA English
SO British Journal of Clinical Pharmacology (1991), 32(5), 569-72
CODEN: BCPHBM; ISSN: 0306-5251
AB The influence of multiple dose administration of omeprazole on the pharmacokinetics of oral digoxin was studied in 10 healthy male volunteers. In a randomized two-way crossover design a single dose of 1 mg digoxin was administered either alone (control) or on day 8 of an 11 day course of omeprazole 20 mg once daily. Plasma digoxin concns. were measured over 96 h after digoxin administration with a [125I]-r.i.a. method. On average, Cmax and AUC values for digoxin were .apprx.10% higher and tmax tended to be shorter during the administration of omeprazole, while the elimination rate constant was unaffected. The increase in AUC(0.96 h) was statistically significant, but within the accepted range for bioequivalence. In two subjects the increase was .apprx.30%. It is concluded that co-treatment with omeprazole causes a minor increase in the absorption of oral digoxin. The magnitude of this effect is not considered to be clin. relevant for the majority of patients.

L9 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1991:614884 CAPLUS
DN 115:214884
TI Antiulcer rectal preparations containing omeprazole
IN Kim, Kwang Sik
PA Hanmi Pharm. Ind. Co., Ltd., S. Korea
SO Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 444625	A1	19910904	EP 1991-102856	19910226 <--
	EP 444625	B1	19940608		
	R: CH, DE, ES, FR, GB, IT, LI, SE				
	CA 2037101	AA	19910828	CA 1991-2037101	19910226 <--

	CA 2037101	C	19970318		
	ES 2057628	T3	19941016	ES 1991-102856	19910226 <--
	JP 04234817	A2	19920824	JP 1991-119605	19910227 <--
	JP 07051503	B4	19950605		
	US 5219870	A	19930615	US 1991-661652	19910227 <--
PRAI	KR 1990-2526	A	19900227		

PI EP 444625 A1 19910904

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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	EP 444625	B1	19940608		
	R: CH, DE, ES, FR, GB, IT, LI, SE				
	CA 2037101	AA	19910828	CA 1991-2037101	19910226 <--
	CA 2037101	C	19970318		
	ES 2057628	T3	19941016	ES 1991-102856	19910226 <--
	JP 04234817	A2	19920824	JP 1991-119605	19910227 <--
	JP 07051503	B4	19950605		
	US 5219870	A	19930615	US 1991-661652	19910227 <--

AB The title preparation comprises (1) omeprazole (I), (2) a mixture of polyethylene glycol-1000, -1540, -4000, or -6000 as a water-soluble base or a mixture of fatty acid, fatty acid ester, and Na lauryl sulfate as a lipid-soluble base, and (3) a stabilizer selected from arginine, lysine, and histidine. When I is orally administered, it is easily decompomposed under the pH of stomach and an enteric-coated preparation requires more time in arriving at the effective serum concentration; therefore, this stabilized composition allows its efficacy by absorption through a neutral or weak alkaline pH media in the rectum. A composition contained I 20, arginine 10, and a mixture of polyethylene glycol 970 mg and its color was unchanged for > 7 days at 50° in 75% relative humidity.

L9 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1991:192453 CAPLUS
DN 114:192453
TI Influence of acid secretory status on absorption of omeprazole from enteric coated granules
AU Andersson, Tommy; Bergstrand, Robert; Cederberg, Christer
CS Res. Lab., AB Haessle, Moelndal, S-431 83, Swed.
SO British Journal of Clinical Pharmacology (1991), 31(3), 275-8
CODEN: BCPHBM; ISSN: 0306-5251
DT Journal
LA English
TI Influence of acid secretory status on absorption of omeprazole from enteric coated granules
SO British Journal of Clinical Pharmacology (1991), 31(3), 275-8
CODEN: BCPHBM; ISSN: 0306-5251
AB To study the absorption of omeprazole under normal acidic conditions in the stomach as well as when the granules are exposed to minimal gastric acid, 8 healthy males were given 20 mg omeprazole as enteric-coated (EC) granules either alone or 2 h after a ranitidine dose of 300 mg, resp. The pH was recorded during the first 4 h in half the subjects in each experiment to document the difference in pH during the absorption phase of omeprazole. The area under the plasma-time curve (AUC) of omeprazole was virtually the same irresp. of whether or not the granules were exposed to gastric acid. However, the maximum plasma concentration was higher and the time to reach Cmax was shorter when omeprazole was administered after a ranitidine dose. Gastric acidity has negligible effect on the AUC of omeprazole, which is directly correlated to the antisecretory effect, when administered as EC granules.
ST omeprazole bioavailability enteric coating granule; gastric juice omeprazole absorption granule

L9 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1991:39637 CAPLUS

DN 114:39637
TI Reduction of eggshell thickness by a proton pump inhibitor, omeprazole
AU Lundholm, C. E.
CS Dep. Pharmacol., Linkoeping Univ., Lindkoeping, S-581 85, Swed.
SO Pharmacology & Toxicology (Oxford, United Kingdom) (1990), 67(3), 269-70
CODEN: PHTOEH; ISSN: 0901-9928
DT Journal
LA English
SO Pharmacology & Toxicology (Oxford, United Kingdom) (1990), 67(3), 269-70
CODEN: PHTOEH; ISSN: 0901-9928
AB About 24 h after a single oral dose of 50 mg of omeprazole per domestic fowl (.apprx.25 mg/kg) the eggshell index (EI) was reduced by 23%. The decrease in EI persisted for 3-4 days, but at a lower rate. The number of eggs was not affected. In these tests omeprazole appeared to exert its action as a potential proton pump inhibitor. It has been suggested that resorption of H+ by the mucosa from the fluid in the shell gland cavity may be an important event in the process of eggshell formation by providing CO32-. It was therefore anticipated that omeprazole might impair the shell formation. The finding that it did in fact do so may support the hypothesis that a proton pump mechanism is involved in the shell formation. Omeprazole did not influence either the K+ metabolism in the shell gland mucosa or the content of K+ in the cavity. The metabolism of Ca was altered, however. There was a significant reduction in the amount of Ca in the lumen of the eggshell gland. Ca in plasma was reduced by 20%, although this reduction was not statistically significant. This would indicate that a reduced amount of Ca reached the shell gland cavity and that omeprazole might interfere with one or both of the principal Ca sources for shell formation in birds, either absorption of Ca from the gastrointestinal tract or resorption of medullary bone from the skeleton.

L9 ANSWER 14 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1989:185703 CAPLUS
DN 110:185703
TI Phase I study of omeprazole. Single-dose and multiple-dose studies
AU Nakashima, Mitsuyoshi; Kanamaru, Mitsutaka; Hashimoto, Hisakuni; Takiguchi, Yoshiharu; Mizuno, Atsuhiro; Kajiho, Tokuaki; Oka, Taichi; Matsuda, Yasuo
CS Sch. Med., Hamamatsu Univ., Handamachi, 431-31, Japan
SO Rinsho Yakuri (1988), 19(4), 667-79
CODEN: RIYADS; ISSN: 0388-1601
DT Journal
LA Japanese
SO Rinsho Yakuri (1988), 19(4), 667-79
CODEN: RIYADS; ISSN: 0388-1601
AB The tolerance and pharmacokinetics of omeprazole (I) a new anti-ulcer drug, in single- and multiple-dose studies in healthy male volunteers were investigated. No abnormal findings in subjective and objective symptoms, blood pressure, heart rate, body temperature, respiratory rate, ECG, or body weight were seen in either study. In the laboratory investigations, some clin. values were outside the normal range. However, these changes were slight and not clin. relevant. Mean plasma concns. of the drug after single doses of 10, 20, and/or 40 mg peaked at 1.3-2.3 h and thereafter declined with half-lives of 1.6-2.8 h. In all the dose groups, <1% of the given dose was excreted as unchanged in the urine, and 12-14% of the dose was excreted as the hydroxylated metabolite in the 24-h urine. Similar plasma concentration profiles were obtained after dosing before breakfast and under fasting conditions in the single-dose study, and no food effects on the absorption of the drug were seen. In the multiple-dose study in volunteers given 20 mg once a day for 7 days before or after breakfast, the time required to reach the peak concentration did not differ between days 1 and 7, and the area under the

plasma concentration curve was greater on day 7 than on day 1. This indicates that the amount of the absorption increased after multiple dosing.

L9 ANSWER 15 OF 15 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1984:583381 CAPLUS
DN 101:183381
TI Oral pharmacokinetics of omeprazole
AU Howden, C. W.; Meredith, P. A.; Forrest, J. A. H.; Reid, J. L.
CS Univ. Dep. Materia Med., Stobhill Gen. Hosp., Glasgow, UK
SO European Journal of Clinical Pharmacology (1984), 26(5), 641-3
CODEN: EJCPAS; ISSN: 0031-6970
DT Journal
LA English
SO European Journal of Clinical Pharmacology (1984), 26(5), 641-3
CODEN: EJCPAS; ISSN: 0031-6970
AB The pharmacokinetics of omeprazole (I) [73590-58-6] were studied in a group of healthy male subjects after single and repeated oral doses of 30 and 60 mg. Absorption of omeprazole from its enteric-coated formulation was unpredictable. There was a highly significant increase in the area under the plasma concentration time curve (AUC) after repeated dosing. Omeprazole increased its own relative bioavailability following repeated dosing. This may be due to inhibition of gastric acid secretion by the drug which is an acid-labile compound